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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/332,659	06/14/1999	FREDERIC ZENHAUSERN	4467-102US	3190

7590 05/12/2005

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EXAMINER

FORMAN, BETTY J

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 05/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/332,659

Applicant(s)

ZENHAUSERN, FREDERIC

Examiner

BJ Forman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 10 March 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1,4-7,9,10,12-14 and 45 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 4-7 9-10 12-14 45 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 30 November 2004 has been entered.

### ***Status of the Claims***

2. This action is in response to papers filed 10 March 2005 in which claims 1 and 45 were amended and claim 42 was canceled. The amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 30 July 2004, not reiterated below, are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are discussed below. New grounds for rejection, necessitated by amendment, are discussed.

Claims 1, 4-7, 9-10, 12-14 and 45 are under prosecution.

### ***Comments***

3. At page 4, third paragraph of the response, Applicant mischaracterizes the interview of February 8, 2005 by stating "The Applicant understands that the only remaining issue, in view of the substance of the interview of February 8, 2005, is whether the subject matter of the instant claims now pending is anticipated under 35 U.S.C. § 102(b) by the disclosure of Van

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Ness et al., '893." While the teaching of Van Ness et al in view of the previously rejected claims was discussed, at no time did the examiner state that the only remaining issue was the Van Ness reference. A review of the Interview Summary provides details of the interview including amendments suggested by the examiner to overcome the prior art.

***Claim Rejections - 35 USC § 112***

**35 U.S.C. 112: first paragraph**

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 4-7, 9-10, 12-14 and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1, from which all other pending claims depend, has been amended to define the claimed method as being drawn to "in-situ monitoring", "*in-situ*" being the newly added limitation. Applicant has not pointed to support for the newly added limitation, and none has been found by the examiner.

Hence, the specification fails to define or provide any disclosure to support such claim recitation.

MPEP 2163.06 notes "If NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in

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the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application.” MPEP 2163.06 further notes “WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT “NEW MATTER” IS INVOLVED. APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE” (emphasis added).

### **35 U.S.C. 112: second paragraph**

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 4-7, 9-10, 12-14 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4-7, 9-10, 12-14 and 45 are indefinite in Claim 1 for the recitation “directly *in situ* monitoring volatile compounds in a gas or vapor phase”. The recitation is indefinite because the phrase “*in situ*” is generally interpreted in the art to mean “in place”. However, the method steps not describe or define a place or location wherein the monitoring occurs. Therefore, it is unclear how the recitation defines the monitoring. Furthermore, the specification provides no guidance on interpreting the “*in situ* monitoring”.

### ***Claim Rejections - 35 USC § 102***

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1, 7, 9-10, 12-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Van Ness et al (U.S. Patent No. 6,312,893, filed 22 July 1997).

Regarding Claim 1, Van Ness et al disclose a method for monitoring a reaction comprising the steps of attaching one or more volatile organic tags a nucleic acid (Column 8, lines 18-65), screening the medium with a multisensor array whereby more than one physico-chemical change of a gas or vapor phase of a nucleic acid is detected (Column 57, line 38-Column 65, line 19) to provide information to produce a signal output, (Column 67, lines 1-19), transferring the signal to a signal processing means for generating a final output, receiving the final output into a pattern recognition means (software program), sorting the information in accordance with a set of class boundaries (analyzer) and monitoring the information "representative" of the identity and amount of nucleic acid (Column 67, lines 20-28 and Claims 1-33). The instant specification broadly defines the "multisensor array" at pages 21-23 as being at least two different sensors (page 21, line 20). Van Ness et al teach numerous sensors including embodiments wherein the multisensor array comprises multiple mass spectrometer detectors (Column 64, lines 44-47) or a quadrupole mass analyzer (Column 59, lines 1-22 and Column 67, lines 6-10). Hence, Van Ness et al teach the multisensor array as claimed. Van Ness et al further teach the method wherein the reaction is monitored in real-time (Column 64, lines 1-4) wherein the reaction monitored is a polymerase chain reaction (Column 65, line 64-Column 66, line 22).

The claim is drawn to a method for directly *in situ* monitoring volatile compounds in a gas or vapor phase from a nucleic acid polymerase chain reaction during the reaction. As

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stated above, the method steps and specification do not define the newly claimed “*in situ* monitoring” so as to define a place (*situ*).

The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111).

The claims are given the broadest reasonable interpretation consistent with the indefinite claim language and specification wherein “*in situ* monitoring” is not defined. Because the claim and specification do not define the place (*situ*) of direct monitoring and because Van Ness et al teach the claimed method steps requiring “real-time” detection, given the broadest reasonable interpretation, Van Ness et al teach the claimed method.

Regarding Claim 7, Van Ness et al disclose the method wherein the multisensor array comprises at least one of a vibrating (Column 57, line 65-Column 58, line 8) or resonant micromechanical device (Column 60, lines 2-23).

Regarding Claim 9, Van Ness et al disclose the method wherein the multisensor array comprises a mass spectrometer (Column 59, lines 1-22).

Regarding Claim 10, Van Ness et al disclose the method wherein the multisensor array comprises an optical sensing probe (Column 63, lines 50-57).

Regarding Claim 12, Van Ness et al disclose the method wherein the information comprises volatile chemical species characteristic of the presence of the nucleic acid (Column 67, lines 1-28).

Regarding Claim 13, Van Ness et al disclose the method wherein the information includes a change in the concentration of nucleic acids i.e. cleavage of the tag from the nucleic acid (Column 63, lines 1-50).

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Regarding Claim 14, Van Ness et al disclose the method wherein the information includes a change in at least one secondary product of the reaction i.e. cleavage of the tag (Column 63, lines 12-23).

### **Response to Arguments**

10. Applicant argues that Van Ness requires separation of the nucleic acid fragments prior to detection and hence does not teach the instant invention of directly *in situ* monitoring a nucleic acid enzymatic reaction during the reaction. Applicant asserts that the instant claims are drawn to a method for directly monitoring without the express need for separation of the nucleic acids before detection, and therefore, none of the claims encompass anything within the disclosure of Van Ness. The argument has been considered but is not persuasive. The instantly claimed methods are drawn to "real-time" detection. Van Ness expressly teaches "real-time" detection (Column 64, lines 1-4). The fact that Van Ness separates fragments does not alter the fact that they monitor the enzymatic reaction in "real-time" as claimed and thereby meet the limitations of the claims. Furthermore, the open claim language "comprising" in the instant claims encompasses any additional steps within the Van Ness reference.

### **Claim Rejections - 35 USC § 103**

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.



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12. Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Ness et al (U.S. Patent No. 6,312,893, filed 22 July 1997) in view of Freidhoff et al (U.S. Patent No. 5,386,115, issued 31 January 1995).

Regarding Claims 4-6, Van Ness et al disclose a method for monitoring a reaction comprising the steps of reacting one or more volatile organic tags with a medium to attach the tag to a nucleic acid product (fragment) (Column 8, lines 18-65), screening the medium with a multisensor array whereby more than one physico-chemical change of a gas or vapor phase of a nucleic acid is detectable (Column 57, line 38-Column 65, line 19) to provide information to produce a signal output, Column 67, lines 1-19), transferring the signal to a signal processing means for generating a final output, receiving the final output into a pattern recognition means (software program), sorting the information in accordance with a set of class boundaries (analyzer) and monitoring the information "representative" of the identity and amount of nucleic acid (Column 67, lines 20-28 and Claims 1-33).

Van Ness et al further teach the method wherein the sensor comprises anyone of many known in the art (e.g. Column 64, line 48-Column 65, line 19) but they do not specifically teach the sensor comprises a semiconductor gas sensor (Claim 4): a metal oxide gas sensor (Claim 5); or a conductive polymer sensor (Claim 7). However, the claimed sensors were well known in the art at the time the claimed invention was made as taught by Freidhoff et al who teach their multisensor array (Fig. 1) comprising a semiconductor gas sensor (Column 3, lines 47-57) comprising a metal oxide gas sensor (Column 5, lines 39-54) and comprising a conductive polymer sensor (i.e. electrodes of conductive material, Column 5, lines 7-17). Freidhoff et al teach their semiconductor gas sensor is small, low power, easily transportable and has the ability to detect multiple constituents simultaneously thereby providing a low cost sensor having wide applications (Column 2, lines 25-30).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the sensor of Freidhoff et al to the gas sensor in the method of

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Van Ness et al based on the preferred teaching and advantages taught by Friedhoff et al. Specifically, one of ordinary skill would have been motivated to use the small, low power, easily transportable sensor of Friedhoff et al for the expected benefits of providing a low cost sensor having wide applications (Column 2, lines 25-30).

### **Response to Arguments**

13. Applicant reiterates the arguments that Van Ness requires a separation step not required in the instant claims. The argument has been considered but not found persuasive because as stated above the “real-time” detection taught by Van Ness is encompassed by the instant claims and further because the method steps do not include method steps limiting the inclusion of separation.

14. Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Van Ness et al (U.S. Patent No. 6,312,893, filed 22 July 1997) in view of Koster et al (U.S. Patent Application Publication No. 2002/0009394, filed 2 April 1999).

Regarding Claim 45, Van Ness et al disclose a method for monitoring a reaction comprising the steps of reacting one or more volatile organic tags with a medium to attach the tag to a nucleic acid product (fragment) (Column 8, lines 18-65), screening the medium with a multisensor array whereby more than one physico-chemical change of a gas or vapor phase of a nucleic acid is detectable (Column 57, line 38-Column 65, line 19) to provide information to produce a signal output, Column 67, lines 1-19), transferring the signal to a signal processing means for generating a final output, receiving the final output into a pattern recognition means (software program), sorting the information in accordance with a set of class boundaries

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(analyzer) and monitoring the information "representative" of the identity and amount of nucleic acid (Column 67, lines 20-28 and Claims 1-33).

Van Ness et al teach the method wherein the reaction is PCR (e.g. Column 18, lines 21-29 and Column 65, lines 64-67) but they do not specifically teach controlling the PCR. However, it was well known in the art at the time the claimed invention was made that PCR is routinely performed by repeated cycles of high and low temperatures controlled by a thermocycler (see Koster et al: ¶ 94-97). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to control the PCR in the method of Van Ness et al based on the well known use of thermocyclers for PCR as taught by Koster et al (¶ 94-97) for the obvious benefit of using routinely practiced methods to thereby obtain desired results i.e. amplification.

15. Claims 1, 7, 9-10, 12, 14 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grow (U.S. Patent No. 5,866,430, issued 2 February 1999) in view of Van Ness et al (U.S. Patent No. 6,312,893, filed 22 July 1997).

Regarding Claim 1, Grow teaches a method for directly, in situ monitoring volatile compounds in a gas or vapor phase (Column 20, lines 32-36), the method comprising screening the medium with a multisensor array (Column 44, lines 53-58 and Fig. 7) to detect a change in gas or vapor phase in real-time (Column 21, lines 60-65) transferring signal to a processing means, generating a pattern of information, sorting the information and monitoring the information in real-time to identify and quantify the nucleic acids (Column 17, line 38-Column 18, line 67) Grow teaches the method is useful for directly monitoring enzymatic synthesis of biologicals (Column 17, lines 41-50) wherein the biologicals include nucleic acids

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(Column 18, line 17 and Claim 2) which clearly suggest their method is useful for polymerase chain reaction (PCR), but Grow does not specifically teach this claimed enzymatic reaction.

However, enzymatic synthesis of nucleic acid via PCR was well known and routinely practiced in the art at the time the claimed invention was made as taught by Van Ness (Column 2, lines 35-37) who teach that PCR is a useful tool for sequencing nucleic acids (Column 2, lines 29-37). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the PCR reaction of Van Ness et al to the enzymatic nucleic acid reaction of Grow for the expected benefit of providing sequence information as desired in the art (Van Ness et al (Column 2, lines 29-37).

Regarding Claim 7, Grow teaches the method wherein the multisensor array comprises or resonant micromechanical device (Column 22, lines 20-45).

Regarding Claim 9, Grow teaches the method wherein the multisensor array comprises a mass spectrometer (Column 22, lines 20-45).

Regarding Claim 10, Grow teaches the method wherein the multisensor array comprises an optical sensing probe i.e. fiber optic probe (Column 22, lines 20-45 and Column 43, lines 30-46).

Regarding Claim 12, Grow teaches the method wherein the information comprises volatile chemical species characteristic of the presence of the nucleic acid i.e. identifies the biological e.g. nucleic acid (Column 20, lines 12-37).

Regarding Claim 14, Grow teaches the method wherein the information includes a changes e.g. a variety of intramolecular and intermolecular reactions are detected (Column 32, lines 1-15).

Regarding Claim 45, Grow teaches the method wherein the reactions are controlled (Column 32, lines 47-67). While Grow does not teach controlling a PCR reaction, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was

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made to apply the controlled enzymatic reaction of Grow to PCR for the expected benefit of optimizing the reaction as they suggest (Column 32, lines 61-67).

### **Conclusion**

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

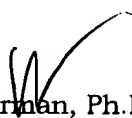
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BJ Forman, Ph.D.  
Primary Examiner  
Art Unit: 1634  
May 10, 2005